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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/021,421	02/10/1998	RUSSEL T. JORDAN	397037	4431

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EXAMINER	
ANDERSON, JAMES D	
ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/021,421	JORDAN ET AL.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7,14-21 and 34-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-7,14-21 and 34-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/26/2008 has been entered.

Formal Matters

Claims 1-3, 5-7, 14-21, and 34-36 are pending and under examination per the claim set submitted 10/31/2007.

Response to Arguments

Applicant's arguments with respect to claims 1-3, 5-7, 20, 21, and 34-36 have been considered but are moot in view of the new ground(s) of rejection. However, in the interest of a complete prosecution history, the Examiner will address Applicant's arguments herein.

Applicant argues that recitation of the function of the claimed compositions carries patentable weight because: (a) this functionality inherently flows from what is claimed and (b) this language clarifies that the claimed composition has this functionality (see page 1 of Remarks filed 6/26/2008). The functionality recited in the claims is "use in treating epithelial lesions" and "capacity for treating at least one type of lesion selected from the group consisting of venereal warts, male veruoca warts, lesions produced by the human papilloma virus, basal cell carcinoma, solar keratosis, Kaposi's sarcoma, eye cancer, sarcoids, sarcoma, malignant melanoma, rectal adenoma, histocytoma, sebaceous adenoma, lung cancer, breast cancer, and colon cancer" (see claim 1). However, the claimed functionality does not result in a physical difference in the composition being claimed. In other words, regardless of what is recited as the functionality, the composition only requires 8-hydroxyquinoline, zinc bonded to 8-hydroxyquinoline, and a carrier. Applicant could recite that the composition is for use in washing walls and it would not change the components that are required to be present in the composition. A recitation of the intended

use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In fact, it is noted that the compositions disclosed in EP '207 are not excluded from the claimed compositions because both are drawn to compositions for use in administration to patients and are thus both pharmaceutical compositions. As such, the Examiner is not persuaded that Applicant's recitation of a use of the claimed compositions should be given patentable weight because it does not result in a structural difference between the claimed invention and the prior art and does not exclude the compositions taught in the prior art (i.e., both are pharmaceutical compositions).

Applicant further argues that he has shown, per the Declaration filed October 26, 2004, the nonequivalence of 8-hydroxyquinoline (claimed) and 8-hydroxyquinoline sulfate (taught in prior art). However, the Examiner notes that the compositions comprising 8-hydroxyquinoline and 8-hydroxyquinoline sulfate differed in more than the active component when tested for the treatment of a lesion. For example, Test 2 Solution containing 8-hydroxyquinoline also contained 40 g $ZnCl_2$ and 5 mL DMSO in a "plasticized base". However, Test 1 Solution containing 8-hydroxyquinoline sulfate contained only 20 g $ZnCl_2$ and no DMSO in an "aquabase". How does Applicant know that the effect of the Test 2 Solution on the lesion was not due to there being 2x more $ZnCl_2$ or by the presence of DMSO? Could the "plasticized base" versus "aquabase" have made a difference? Thus, the Examiner cannot accept that the different results shown for the Test 1 and Test 2 solutions can be attributable only to the presence of 8-hydroxyquinoline versus 8-hydroxyquinoline sulfate. In addition, the functional equivalence of 8-hydroxyquinoline and 8-hydroxyquinoline sulfate is that they are known antifungal agents. As such, even if it were shown that 8-hydroxyquinoline treats lesions and 8-hydroxyquinoline sulfate does not, this does not negate the fact that these two compounds are both antifungal agents and thus reasonably substituted one for the other in the prior art compositions.

Lastly, Applicant argues that the claimed composition possesses unexpected properties that are not found in the compositions expressly taught in the prior art. However, the prior art teaches that the compositions disclosed therein "enhance the skin or mucous membrane penetration and retention of the pharmacologically active agent" (Abstract of EP 0 506 207).

Applicant has not shown that a composition comprising 8-hydroxyquinoline does not have this effect as disclosed in EP '207. In fact, the invention of EP '207 is not dependent on the pharmaceutically active agent, rather it is the presence of a water-soluble zinc-containing compound in a topical pharmaceutical composition that results in the enhanced skin or mucous membrane penetration and retention of a pharmacologically active agent. As such, the fact that such a composition as taught in the prior art also has the additional effect of treating lesions, treating acne, or treating foot odor does not make such compositions patentable over the prior art by simply reciting a new, unappreciated property or intended use thereof.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5-7, and 14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over **EP 0 506 207 A2** (Published 9/30/1992) (prior art of record) in view of **The Merck Index 12th Edition** (1996, Merck & Co., publ., pages 832 (Entry 4890)) (prior art of record).

EP '207 discloses the use of water-soluble zinc-containing compounds in topical pharmaceutical compositions containing pharmacologically active agents to enhance the skin or mucous membrane penetration and retention of the pharmacologically active agent (Abstract). The preferred water-soluble zinc-containing compounds include zinc chloride as recited in the

instant claims 5 and 6 (page 2, lines 42-43). Said water-soluble zinc-containing compounds are disclosed to dissociate in the topical vehicle so as to provide zinc ions for complexation or chelation with the pharmacologically active agents present in the vehicle (page 3, lines 10-12). Zinc-containing compounds are preferably present in an equimolar ratio with the pharmacologically active agents, thus meeting the limitation of instant claims 2-3 (*id*. at lines 24-25). With respect to the instantly claimed concentration of 8-hydroxyquinoline of at least 5 percent, it would have been obvious to use the same amount of active agent as the amount of the zinc-containing compound because the reference discloses equimolar ratios. Normally, use of equimolar amounts of a zinc-containing compound and pharmacologically active agent will not involve the use of escharotic amounts of zinc chloride and less than 35% zinc chloride is disclosed to be an upper limit when no escharotic effect is desired (*id*. at lines 28-31). This upper limit meets the limitation "ranging up to forty percent by weight" as recited in instant claim 5 and "less than an amount that produces an eschar in healthy mammalian tissues" as recited in instant claim 1. Other ingredients, including stability-enhancing agents and antioxidants may be added to the disclosed compositions (*id*. at lines 35-36). With respect to the carriers recited in claim 14, the reference discloses that typical carriers include water, gel-producing materials, propylene glycol, sorbitol, etc. (page 5, lines 40-43).

With respect to the addition of the instantly claimed 8-hydroxyquinoline, EP '207 suggests that antifungal agents are suitable pharmacologically active agents for use in the disclosed compositions and discloses 8-hydroxyquinoline sulfate as a suitable antifungal agent (page 4, lines 9-31). While 8-hydroxyquinoline is not explicitly recited in the list of antifungal agents in EP '207, it is noted that Applicants disclose at page 2, lines 3-22 of their specification that 8-hydroxyquinoline is a known antifungal agent and chelating agent (see especially lines 12-14). Such is also evidenced by The Merck Index, which teaches that 8-hydroxyquinoline is a known "fungistat" used as an "antiseptic". Thus, it would have been obvious to one of ordinary skill in the art to use 8-hydroxyquinoline as an antifungal agent in the compositions disclosed in EO '207.

Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to formulate a composition comprising 8-hydroxyquinoline and a chelatable metal agent such as zinc chloride. The motivation to do so is found throughout EP

'207 wherein compositions comprising zinc chloride and pharmacologically active agents, including antifungal agents, are disclosed. As such, it would have been obvious to one of ordinary skill in the art that any antifungal agent, including the instantly claimed 8-hydroxyquinoline, could have been reasonably incorporated into the compositions disclosed in EP '207. Applicants' discovery that compositions comprising 8-hydroxyquinoline and zinc chloride can be used to treat epithelial lesions does not constitute a patentable distinction over the compositions disclosed in the reference. This is because a composition comprising 8-hydroxyquinoline and zinc chloride, as reasonably suggested and motivated by EP '207, is capable of performing the use recited in the instant claims.

With regard to claim 7, which recite a composition set forth in claim 1 "in combination with necrotic tissue from a lesion of said group produced by the action of said composition upon the lesion", it is noted that EP '207 teaches pharmaceutical preparations containing zinc ions and pharmacologically active agents are "injected directly into diseased tissues, particularly solid tumors" (page 5, lines 34-38). Thus, EP '207 reasonably suggests a composition of the invention "in combination" with necrotic tissue.

Claim 15 is rejected under 35 U.S.C. § 103(a) as being unpatentable over **EP 0 506 207 A2** (Published 9/30/1992) in view of **The Merck Index 12th Edition** (1996, Merck & Co., publ., pages 832 (Entry 4890)) as applied to claims 1-3, 5-7, and 14 above, and further in view of **USP No. 4,780,320** (Issued Oct. 25, 1988) (newly cited).

EP '207 and The Merck Index disclose as discussed *supra*. USP No. 4,780,320 is provided as evidence that the Pluronic series of polyoxypropylene-polyoxyethylene copolymers, marketed by BASF Wyandotte, Parsippany, N.J., contains several suitable examples if gelling polymers, such as Pluronic F127 as disclosed in Applciant's specification (Example 1). These polymers are compatible with many commonly used pharmaceutical materials, and have been approved by the FDA for medical use (col. 7, lines 31-46). Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art to use a gel comprising a polyoxyethylene ether derivative of propylene glycol (i.e., a Pluronic gelling polymer) as a carrier for claimed compositions. The skilled artisan would reasonably expect that such a gelling polymer would be a suitable carrier for pharmaceutical agents as taught in USP No. 4,780,320.

Claims 16-18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over **EP 0 506 207 A2** (Published 9/30/1992) in view of **The Merck Index 12th Edition** (1996, Merck & Co., publ., pages 832 (Entry 4890)) as applied to claims 1-3, 5-7, and 14 above, and further in view of **The Merck Index 12th Edition** (1996, Merck & Co., publ., pages 551 & 925-926) (prior art of record).

EP '207 and The Merck Index disclose as discussed *supra*. The Merck Index is provided as evidence that lecithin is an edible and digestible surfactant and emulsifier of natural origin used in pharmaceuticals and cosmetics (page 926). Further, dimethyl sulfoxide is disclosed as a penetrant carrier to enhance absorption (page 551). Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art to use lecithin and/or dimethyl sulfoxide in a carrier for pharmaceutically active agents. The skilled artisan would reasonably expect that lecithin and/or dimethyl sulfoxide would be effective in increasing the absorption of the topical compositions disclosed in EP '207.

Claims 19-21 and 34-36 are rejected under 35 U.S.C. § 103(a) as being unpatentable over **EP 0 506 207 A2** (Published 9/30/1992) in view of **The Merck Index 12th Edition** (1996, Merck & Co., publ., pages 832 (Entry 4890)) as applied to claims 1-3, 5-7, and 14 above, and further in view of **USP No. 3,637,772** (Issued Jan. 25, 1972) (newly cited).

EP '207 and The Merck Index disclose as discussed *supra*. EP '207 teaches the addition of antioxidants as additional components to the disclosed compositions (page 3, lines 35-36). EP '207 does not explicitly teach the antioxidants nordihydroguiaretic acid and ascorbic acid as recited in claims 19-21 and 34-36. However, USP No. 3,637,772 teaches that antioxidants are employed to delay the decomposition of oxidation sensitive materials and the most frequently used antioxidants include nordihydroguiaretic acid (col. 1, lines 20-35). Ascorbic acid is taught to also be used in combination with other antioxidants as a synergist (col. 1, lines 36-37 and 53). Thus, it would have been obvious to one of ordinary skill in the art to use nordihydroguiaretic acid and/or ascorbic acid as the antioxidant component suggested and motivated by EP '207. The skilled artisan would also have been imbued with at least a reasonable expectation that such antioxidants could be used as carriers for the pharmaceutical composition of EP '207.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614